Preventive Effects of Sea Cucumber-Derived Fucoidan on

Helicobacter pylori-Induced Gastritis: Mechanistic Investigation

Based on Regulation of Gut Microbiota and Metabolic Products

Junhan Cao^{a,b,c}, Kai Wang^e, Mengke Yao^{c,d}, Qing Zhang^d, Kuan Luf, Changfeng Qud,

Wancui Xief, Hua Yina*, Xinpeng Wangb*, Jinlai Miaoc,d*, Changhu Xuec

^aR&D center, Tsingtao Brewery Co., LTD, Qingdao, 266207, China;

^bSchool of Rehabilitation Sciences and Engineering, University of Health and

Rehabilitation Sciences, Qingdao, 266113, China;

^cCollege of Food Science and Engineering, Ocean University of China, Qingdao,

266003, China;

^dQingdao Key Laboratory of Marine Natural Products Research and Development

Laboratory, First Institute of Oceanography, Ministry of Natural Resources, Qingdao,

266061, China;

^eQingdao Hospital, University of Health and Rehabilitation Sciences (Qingdao

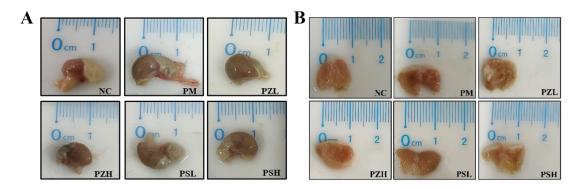
Municipal Hospital), Qingdao, 266071, China;

^f Homey Group International Inc., Rongcheng, 264305, China.

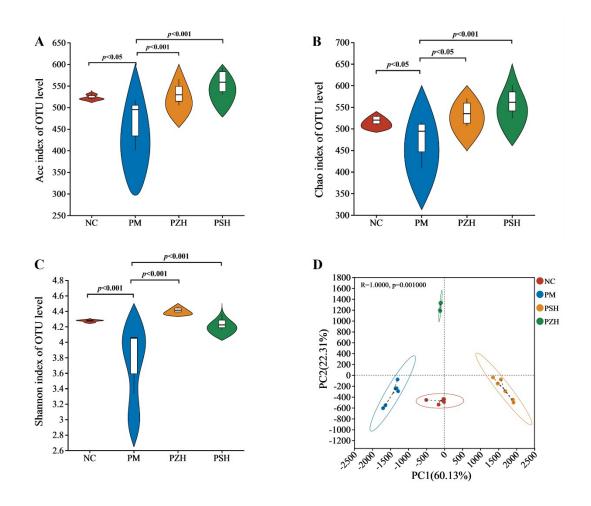
*Corresponding authors:

Email: miaojinlai@fio.org.cn

Supplementary Figures

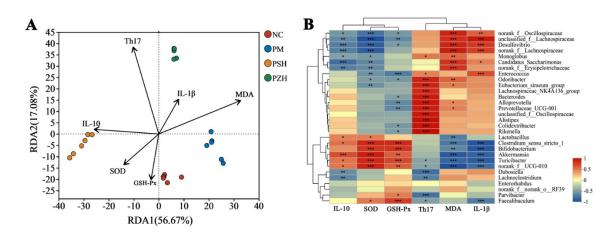


Supplementary Fig. 1 Macroscopic image (A) and anatomical diagram (B) of the gastric tissue.

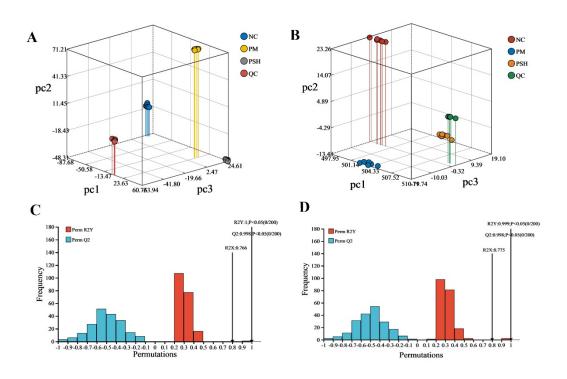


Supplementary Fig. 2 Analysis of diversity of gut microbiota. (A) Kruskal-Wallis H test for the Ace index; (B) Kruskal-Wallis H test for the Chao index; (C) Kruskal-Wallis H test for the Shannon index; (D) PCA analysis at the OTU level. Each group comprised

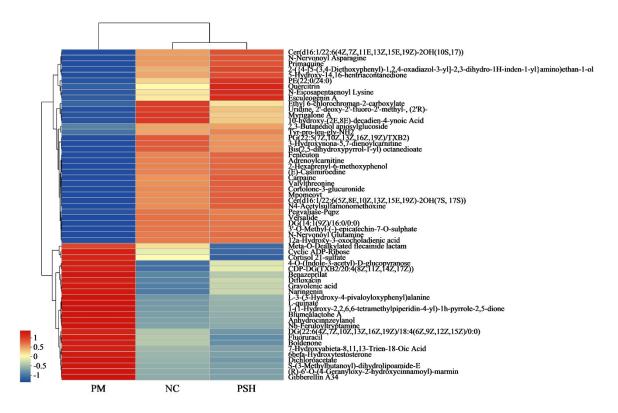
n = 6 biologically independent mice. p < 0.05 indicates significant differences between groups.



Supplementary Fig. 3 (A) RDA analysis of gut microbiota at the genus level; (B) Correlation analysis between inflammatory factors and gut microbiota.

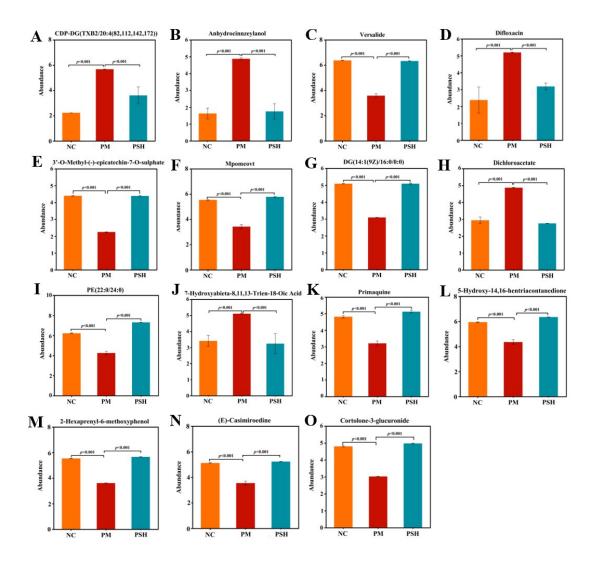


Supplementary Fig. 4 3D-PCA diagram of metabolites in the prevention group in positive (A) and negative (B) modes and PLS-DA replacement test in positive (C) and negative (D) modes.



Supplementary Fig. 5 Cluster heatmap analysis of common differential metabolites of

PM vs NC and PSH vs PM metabolic set.



Supplementary Fig. 6 Key metabolites. (A) The relative content of CDP-DG (TXB2/20:4(8Z,11Z,14Z,17Z)); (B) The relative content of Anhydrocinnzeylanol; (C) The relative content of Versalide; (D) Tthe relative content of Difloxacin; (E) The relative content of 3'-O-methyl-(-)-epicatechin-7-O-sulphate; (F) The relative content of Mpomeovt; (G) The relative content of DG (14:1(9Z)/16:0/0:0); (H) The relative content of Dichloroacetate; (I) The relative content of PE (22:0/24:0); (J) The relative content of 7-hydroxyabieta-8,11,13-rien-18-oic acid; (K) The relative content of Primaquine; (L) The relative content of 5-hydroxy-14,16-hentriacontanedione; (M) The relative content of 2-hexaprenyl-6-methoxyphenol; (N) The relative content of (E)-

casimiroedine; (O) The relative content of cortolone-3-glucuronide. p<0.05 indicates significant differences between groups.